UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,251	10/20/2006	Luca Gianni	13566.105020	7104

65989 7590 01/24/2008

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
4173	

NOTIFICATION DATE	DELIVERY MODE
01/24/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,251	GIANNI ET AL.	
	Examiner	Art Unit	
	Jonathan Lau	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20pgs/12May2006, 13Nov2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/GB04/50025, filed 12 Nov 2004; and claims benefit of foreign priority document UNITED KINGDOM 0326486.8, filed 14 Nov 2003.

Claims 1-15 and 19 are pending in the current application. Claims 1-15 and 19 are examined on the merits herein.

Election/Restrictions

Applicant's election of Group I, claims 1-15, in the reply filed on 13 Nov 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election of species of sarcoma in the reply filed on 13 Nov 2007 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed 13 Nov 2007 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Reference 21, Takahashi et al., "Sequence-dependent Synergistic Cytotoxicity of Ecteinascidin-743 and Paclitaxel in Human Breast Cancer Cell Lines in Vitro and in Vivo," Cancer Research, 62:6909-6915 (Dec. 1, 2002), of the IDS filed 13 Nov 2007 has not been considered because a copy of the reference non-patent literature publication has not been submitted.

The information disclosure statement filed 13 Nov 2007 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

The non-patent literature publication, Takahashi et al., "Sequence-dependent Enhancement of Cytotoxicity Produced by Ecteinascidin 743 (ET-743) with Doxorubicin or Paclitaxel in Soft Tissue Sarcoma Cells, Clinical Cancer Research, 7, p3251-3257, 2001, is not listed on an IDS, and the information referred to therein has not been considered.

Specification

The disclosure is objected to because of the following informalities: The minor typographical error that doxorubicin is defined to have the abbreviation "doxo" but is thereafter referred to as both "doxo" and "Doxo". For example, see page 10, line 5 and page 14, line 10 for definition of the abbreviation, page 11, line 7 for usage of "Doxo" and page 14, line 24 for usage of "doxo". For consistency, the capitalization should be consistent with the defined abbreviation unless capitalized at the beginning of a sentence.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8, 11, 14, 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi et al. (WIPO publication WO 02/36135, published 10 May 2002, provided by Applicant in IDS filed 2 May 2006) and Bowman et al. (WIPO publication WO 00/69441, published 23 Nov 2000, provided by Applicant in IDS filed 2 May 2006), which is incorporated-by-reference into Takahashi et al. (Takahashi et al. page 1, lines 5-7).

Takahashi et al. discloses the method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma (page 2, lines 26-29), specifically envisioning treating a human (page 4, lines 11-12). Takahashi et al. specifically references WO 00/69441 (Bowman et al.) for dosing schemes for ET-743 (page 5, lines 12-13). Bowman et al. discloses the recommended doses for ET-743 of 500 or 1000 micrograms per m2, or 0.5 or 1.0 mg/m^2 (Bowman et al. page 13, lines 16-17 and 20-21). The method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma in a human 0.5 or 1.0 mg/m^2 doses for ET-743 anticipates instant claims 1, 14, 15 and 19. Takahashi et al. discloses the drugs provided as a separate composition for administration at different times (page 1, lines 12-13), anticipating instant claim 3. Takahashi et al. discloses administering ET-743 after administering doxorubicin (page 21, lines 13-14), which is to say administering doxorubicin prior to the administration of ET-743, anticipating instant claim 4. Takahashi et al. discloses administration of the compounds by intravenous infusion, with infusion times of up to 24 hours and 2-6 hours preferred (page 4, lines 25-26), anticipating instant claims 5-7. Compared to an infusion time of 24 hours, 2 hours is about 1 hour or 3 hours. Takahashi et al. discloses infusions carried out at suitable intervals of 2 to 4 weeks (page 5, lines 2-3), anticipating instant claim 8. Takahashi et al. discloses administering 0.1 mg/kg ET-743 after 10 mg/kg doxorubicin into a mouse model (page 6, line 8). As evidenced by Friereich et al. (Cancer Chemotherapy Reports, 1966, 50, p219-245, cited in PTO-892), a conversion factor of 3.0 is used to convert mg/kg to mg/m^2 in the mouse model (page 238, right

column, lines 3-20). Therefore Takahashi et al. discloses administering 0.3 mg/m^2 ET-743 and 30 mg/m^2 doxorubicin, anticipating instant claim 11.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (WIPO publication WO 02/36135, published 10 May 2002, provided by Applicant in IDS filed 2 May 2006) and Bowman et al. (WIPO publication WO 00/69441, published 23 Nov 2000, provided by Applicant in IDS filed 2 May 2006), which is incorporated-by-reference into Takahashi et al. (Takahashi et al. page 1, lines 5-7) in

view of Dorr and Von Hoff (Cancer Chemotherapy Handbook, 1994, Appleton & Lange, 2nd ed, p395-416).

Takahashi et al. discloses the method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma (page 2, lines 26-29), specifically envisioning treating a human (page 4, lines 11-12). Takahashi et al. specifically references WO 00/69441 (Bowman et al.) for dosing schemes for ET-743 (page 5, lines 12-13). Bowman et al. discloses the recommended doses for ET-743 of 500 or 1000 micrograms per m2, or 0.5 or 1.0 mg/m^2 (Bowman et al. page 13, lines 16-17 and 20-21). The method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma in a human 0.5 or 1.0 mg/m^2 doses for ET-743 anticipates instant claims 1, 14, 15 and 19. Takahashi et al. discloses the drugs provided as a separate composition for administration at different times (page 1, lines 12-13), anticipating instant claim 3. Takahashi et al. discloses administering ET-743 after administering doxorubicin (page 21, lines 13-14), which is to say administering doxorubicin prior to the administration of ET-743, anticipating instant claim 4. Takahashi et al. discloses administration of the compounds by intravenous infusion, with infusion times of up to 24 hours and 2-6 hours preferred (page 4, lines 25-26), anticipating instant claims 5-7. Compared to an infusion time of 24 hours, 2 hours is about 1 hour or 3 hours. Takahashi et al. discloses infusions carried out at suitable intervals of 2 to 4 weeks (page 5, lines 2-3), anticipating instant claim 8. Takahashi et al. discloses administering 0.1 mg/kg ET-743 after 10 mg/kg doxorubicin into a mouse model (page 6, line 8). As evidenced by Friereich et al. (Cancer Chemotherapy Reports, 1966, 50, p219-245, cited in PTO-892), a conversion

factor of 3.0 is used to convert mg/kg to mg/m^2 in the mouse model (page 238, right column, lines 3-20). Therefore Takahashi et al. discloses administering 0.3 mg/m^2 ET-743 and 30 mg/m^2 doxorubicin, anticipating instant claim 11. Takahashi et al. specifically references WO 00/69441 (Bowman et al.) for dosing schemes for ET-743 (page 5, lines 12-13). Bowman et al. discloses administration of ET-734 performed in cycles of 3 weeks, or 21 days, with the drug administered in the first days of each cycle, and schedule adjustments performed as needed depending on the individual patient (Bowman et al. page 12, lines 1-6), addressing instant claims 9 and 10. Takahashi et al. discloses the correct dosage of the compounds will vary according to the particular formulation, mode of application, *situs*, host, and tumor being treated (page 5, lines 6-10), addressing instant claims 11-13. Bowman et al., incorporate-by-reference into Takahashi et al., discloses the recommended doses for ET-743 of 0.5 mg/m^2 (Bowman et al. page 13, lines 16-17 and 20-21), which when compared a dose of 1.65 mg/m^2 disclosed by Bowman et al. is about 0.6 mg/m^2 or 0.7 mg/m^2, addressing instant claims 12 and 13.

Takahashi et al. does not specifically disclose doxorubicin administered with a dose of 40-80 mg/m^2, about 60 mg/m^2 or about 50 mg/m^2, disclosed in instant claims 2, 12 and 13 respectively. Takahashi et al. does not specifically disclose the infusion of doxorubicin carried out once every 21 days, disclosed in instant claim 9. Takahashi et al. does not specifically disclose the method wherein the infusion of doxorubicin is carried out on day 1 and the infusion of ET-743 on days 1 and 8, every 21 days, disclosed in instant claim 10.

Dorr and Von Hoff teaches dosing guidelines for doxorubicin of 60-75 mg/m^2 administered every 3 weeks (page 399, table on lines 38-45), or 21 days. Compared to a dose of up to 120 mg/m^2 (page 399, left column, lines 10-13), a dose of 60 mg/m^2 is about 50 mg/m^2.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Takahashi et al. using the dosage of doxorubicin of about 50 mg/m^2 administered every 3 weeks taught by Dorr and Von Hoff. Dorr and Von Hoff teaches guidelines for dosing, which would motivate one of ordinary skill in the art at the time of the invention to follow the guidelines. Takahashi et al. discloses the correct dosage of the compounds will vary according to the particular formulation, mode of application, *situs*, host, and tumor being treated (page 5, lines 6-10). Bowman et al. discloses administration of ET-734 performed in cycles of 3 weeks, or 21 days, with the drug administered in the first days of each cycle, and schedule adjustments performed as needed depending on the individual patient (Bowman et al. page 12, lines 1-6). Therefore one of ordinary skill in the art at the time of the invention would be motivated to practice the method wherein the infusion of doxorubicin is carried out on day 1 and the infusion of ET-743 on days 1 and 8, every 21 days.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 19-20 of commonly assigned copending Application No. 11/577,790. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-11 and 19-20 of copending Application No. 11/577,790 are drawn to a method of treating cancer in a human comprising administering ET-743 and a Pegylated Liposomal form of the anthracycline Doxorubicin. Instant claims 1-9, 11-13 and 19 are drawn to the method of treating cancer in a human comprising administering ET-743 and doxorubicin. The instant specification discloses one non-limiting embodiment wherein the doxorubicin does not take the form of doxorubicin in the Pegylated Liposomal form (page 8, lines 8-10). However, this disclosure also leads one to immediately envision opposite, the embodiment wherein the doxorubicin does take the form of doxorubicin Pegylated Liposomal form. Claims 2 and 3 recites the limitation of instant claim 3. Claim 4 recites the limitation of instant claim 4. Claim 5 recites the

limitation of instant claim 5. Claim 6 obviates the limitation of instant claim 6. Claim 7 obviates instant claim 7. Claim 8 obviates instant claims 8 and 9. Claims 10 and 11 obviates the dosage ranges of instant claims 1 and 2. Instant claim 2 discloses the method wherein doxorubicin is administered with a dose of 40 mg/m^2, which is about 30 mg/m^2 when compared to the disclosed value of 80 mg/m^2, obviated by the doxorubicin dosage of claim 11 of copending Application No. 11/577,790.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 33 and 34 of copending Application No. 9/787,461. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 34 of copending Application No. 9/787,461 recites the combination of method of treating cancer in a human comprising administering ET-743 at a dose level of 0.5 mg/m^2 and at least one additional drug selected from the a list including a drug that targets DNA. The specification of copending Application No. 9/787,461 envisions the drug that targets DNA to be doxorubicin (page 8, lines 24-25), obviating instant claims 1 and 19. The specification of copending Application No. 9/787,461 envisions the drugs to be provided as a separate composition for administration at a different time, obviating instant claim 3.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is (571) 270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718 or Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSL

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614